From the seat of heat and intelligence to regular heart activity as automatic movement: progress in cardiology up to 1900 from a Dutch perspective

C. van Tellingen

The development in cardiovascular anatomy and physiology is described from a Dutch perspective. The newly formed Republic in the 17th century, with its pragmatism and business-like character, became an ideal breeding ground for Descartes' new philosophy. His separation of body and soul provided a mechanistic model of body structure and formed a firm basis for anatomical and physiological research to become catalysts for a tempestuous growth and progress in medicine. (*Neth Heart J* 2009;17:130-5.)

Keywords: medical history, cardiovascular physiology, cardiovascular progress

Embarking on a voyage that should take us along the landmarks in Dutch cardiology, it is mandatory to realise that there is no such thing as a separate national development in medicine. The growth of idea, with its rise and fall, always was and always will be a continuous interaction between learned men and their surroundings. It gradually evolves until the moment that a *primus inter pares* clarifies its nature. The heart captured human imagination from the earliest days onwards: 'I touched his heart but it does not beat at all'.[1] This statement, attributed to Gilgamesh witnessing the death of his best friend, is noted in the Mesopotamian Epic of Gilgamesh in 2600 BC and constitutes the earliest reference to an understanding of the heart and its motion as the life-sustaining organ of the body.

C. van Tellingen
Cardiologist, Roosendaal, the Netherlands

Correspondence to: C. van Tellingen
Duke Ellingtonlaan 23, 4702 KG, Roosedaal, the Netherlands
E-mail: cvantellingen@dukebox.demon.nl

The beginning

In the millennia to come, astonishment was to be replaced by reasoning and interfering.

Roman medicine with Galen as its most famous exponent theoretically founded the basis of diagnosis and therapy in the earliest days of medicine in our region too. *De pulsibus ad tirones* contain Galen's four well-known treatises on the pulse as a means of diagnosis and prognosis.[2] He also conducted comparative studies on the anatomy of the heart in different sized animals and his anatomical skills were unsurpassed in the ancient world.[3] Galen's thoughts and systematic approach were still standing in the 16th century and his theorems were discussed until the 19th century, giving some idea of the importance of his writings throughout the ages. Initially his

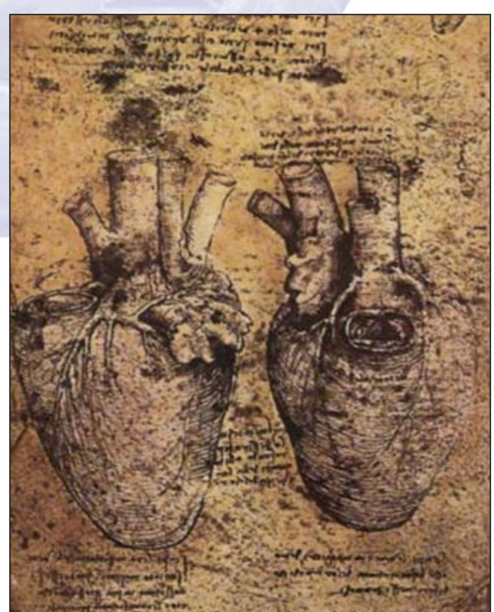

Figure 1. Da Vinci's detailed anatomical drawings still stand today.

message of observation and experimentation was largely lost and for that reason his theories became more like a dogma imposed on generations of physicians to come.

Cardiovascular dynamics in its nature profited most from new insight when Descartes (1596-1650), who lived and worked for 20 years in the Dutch republic, declared that the body of a man was a machine where a spirit dwelt. This mechanical approach led to the assumption that causes were necessarily forms of pushes and pulls and all effects the consequence of pushes and pulls. However, he never challenged the Galenic concept of the heart being the source of natural heat. Nevertheless, Descartes' physiology seems logical and efficient enough to settle with the classic concepts. Literally everything was open to debate and that very fact stimulated the scholastic Western world to reconsider, reviewing each other in controlled experiments to separate chaff from wheat. And anatomy as a skill and a profession was the natural arena of the time to settle differences and – not insignificant – to show off ones learning and accomplishments.

Before dealing with an alleged Dutch experience, we have to mention William Harvey (1578-1657), considered to be one of the great icons of 17th century thinking. His popularity owed everything to one of the great scientific discoveries of the time: that of the circulation of blood. Nevertheless despite his view on propulsion of the blood by means of contraction, he too stayed close to Galen's concept of the heart as the source of natural heat. Harvey's sensational discovery was made known to the world in 1628 in *De Motu Cordis* and this event seems the logical starting point to look for a Dutch view on matters of the heart.

The dawning of a new age

Up until the 16th century, academic medical education leant heavily on Hippocrates (*Corpus Hippocraticum*), the Roman scholar Galen, and Avicenna, a Persian physician, scholar and philosopher from the middle ages. In the balance between sickness and health, the focus lay on the four humours identified as black bile, yellow bile, phlegm, and blood. All diseases and disabilities resulted from an excess or deficit of one of these four humours. The heart was thought to pump blood through the body, generate heat and store intelligence. Andreas Vesalius (1514-1564) and his anatomical drawings contributed much to a better understanding of the human body and its different organs. He was the first to challenge Galen, when he proved the absence of so-called *communicantes* or connections between the left and right ventricle, generally regarded as the cornerstone of Galen's representation of the circulation of blood. His revolutionary work was quite easily adapted to the 'young' universities of the Lowlands, which did not carry the burden of heritage as much as their counterparts in especially France, Italy and Spain where Catholicism held its own view on compassion and cures. After the Spanish domination, Leiden University was founded in 1575. Pieter Pauw (1536-1599) became one of its first professors and set up the first *Theatrum Anatomicum* in the newly formed republic in 1597. Anatomical lessons were thought to be quite lucrative at the time. One lesson, given in 1647 by Tulp in Amsterdam over a five-day period, brought in 229 guilders and 9 stuivers (the odd € 2335 today)[4] which not only paid for the expenses but underwrote a fine torchlight procession and grand dinner upon conclusion. Tulp used to convey two moral messages to the crowds that attended these lessons to give his performance a distinctive stamp: all humans are mortal and the glory of God could be seen in the extraordinarily complex handiwork of his creation.[5] For a while, anatomy was 'hot' and anatomic skills the standard to measure and decide upon success and prestige.

When William Harvey cleaned up the medical barn, filled with content, complacency and dogmatism influenced by religious interest, his work was controversial and not very enthusiastically received in the academic world of the day. That did not refer to Anthony van Leeuwenhoek (1632-1723), who developed an attachment to his microscope, a glass tube, the so called 'eel-viewer'. This enabled him to make scientific researches into the glass-eel and so he visualised the heart (*in vivo*) pumping blood. In this way he was the first to give direct evidence to Harvey's observations and deductions.[6] Johannes de Wale (1604-1649), professor in Leiden, was one of the few at the time who verified Harvey's experimental research too. Johan van Beverwijck (1594-1649), a well-known physician from Dordrecht, and a young Francois de le Boe Sylvius (1614-1672), who would become one of the most distinguished and liberal scholars of his time, also deserve credit for the fact that they agreed with the opinions and ideas of Harvey in an early stage.[7] Finally Steven Blankaart (1650-1704), spouting up blood vessels to prove the existence of a capillary system as was already suggested by Leonardo da Vinci, should be mentioned. Unfortunately he failed to recognise the true significance of his finding but nevertheless contributed his mite to the great adventure that lay in front of him and his contemporaries.[8]

Sylvius initially graduated at Basel, Switzerland, in 1637 and came to Leiden in 1638. There he set up anatomical demonstrations on animals which were extended to include physiological experiments, among which a series of unique experiments to demonstrate his theory of blood circulation in the dog.[9] Despite the apparent success of this practice there was for some time commotion in the Calvinistic republic not as far as the circulation of blood was concerned but rather on the working of the heart itself. Voetius (1589-1676), a theologian and the first professor of Utrecht University, was an exponent of those who had a distinct aversion for renewal in philosophy and natural science.[10] After a while this fate was decided and eventually Harvey got his pedestal, as is quite evident from the words of Albinus (1697-1770), one of the great anatomists of his time, who in 1736 delivered a copy of the anatomical works of William Harvey to Leiden University. In the preface of this work Albinus mentioned the merits of physiologists: 'It is sufficient to put one man on the stage, Harvey and his *de Motu Cordis,* in which he gave such an explanation of nature that I do not fear to make an example of him before anyone else'.[11] Although new discoveries were initially considered to be modernisms, not to be taken seriously, and some of the scientific elite rather desperately clung to the old Aristotelian descriptive model despite undeniable flaws, more and more saw in Descartes the new champion of reason. His explanatory kind of reasoning seemed far more efficient and simple than the old views. The ban was broken and the study of anatomy and physiology became catalysts for further growth and progress in medicine.

Jan Swammerdam (1637-1680), at the time a young student in Leiden, held great admiration for Harvey. In his turn he designed all sorts of experiments to reveal the true nature of respiration. His observations that the heart taken from a frog pulsated for 16 hours and that touching the nerve of a muscle in a frog caused muscular contraction even when the limb involved was detached, were initially by-products of his research on respiration, but soon became revolutionary in their own right. His findings led his fellow student Niels Stensen (1638-1686), a Dane who came to Holland to improve his anatomical skills, to the conclusion that the heart too was a muscle. When he dissected a young raven in 1662 he witnessed that the heart continued to contract despite the incision. He then noticed that ligation of the caval veins stopped cardiac activity which was restored after letting the blood in again. He proved that the heart even continued to contract outside the body and then combined his own observations with the findings of Swammerdam. The heart too was a muscle acting on nerval stimuli but independently from cerebral activity.[12] This revolutionary concept had of course a dramatic effect on the scientific establishment. Its implication was evident and was a finishing stroke for the physiological concepts of both Galen and Descartes, where the heart held a central place as the seat of natural heat.

The experience of ignorance and faith

What was the effect on clinical medicine of these revolutionary findings? The answer is short and concise: for the time being none whatsoever. Although physicians did not have the faintest idea of what they were doing, their remedies for a number of ailments were founded on centuries-old empirical experience and in a way they were quite successful. Over and above this, there was a lot of interest for the possible pharmaceutical effects of newly discovered herbs and plants from the New world. Cornelis Bontekoe (1647-1685), for instance, propagated in his treatise on tea the use of it as a miraculous remedy to keep the blood warm and clear.[13]

New physiological insight, how important it may now seem to us who are fully aware of the ultimate course of events, at the most brought some unrest and (theological) debate but did not contribute very much to everyday medical practice, although a mechanical input in the archaic concept of the humours was generally accepted. So ordinary physicians and academics as well tended to deny the potential of these new ideas, especially when they could not be incorporated in the existing (Hippocratic) views. Change may be inevitable but it had to prove itself every inch of the way and during this process there was of course a lot of debate among the very advocates of a new philosophy too. These so-called Cartesians had to abide their time and as a consequence there was a longer period of academic turmoil and dispute, which lasted until the 19th century!

To capture the state of affairs in such a changing environment as the 18th century, where the pros and cons of a whole new mindset towards sickness and health hung in the balance, we have to rely on the available undisputed sources of the time as landmarks of learning and doing. At least in the Western world, Herman Boerhaave (1668-1738) is considered to be one of the hallmarks of medicine. His aphorisms, already published in 1710 and reprinted with additions again and again until 1791, may very well serve as the state of the art in medicine at the time. It is not coincidental that the title of this resume of his lectures related directly to the famous Hippocratic aphorisms, of old subject of medical examination. Although his starting point was a mechanical model of body structure and despite implementation of some aspects of iatrochemistry with emphasis on the importance of a specific chemical balance of bodily fluids, Boerhaave was a convinced follower of the Hippocratic writings and values and did not hold much with renewers. His funeral oration gave ample evidence for his opinion: *He (Boerhaave) noticed that the easy indolence of some and the proud conceit of others took away the arch-physician (Hippocrates) from his rightly deserved pedestal. Indeed, the youth dedicated to exercise in medicine were distracted from this most original source through the authority and example of great men too.* Boerhaave considered it his duty to bring his students back to Hippocrates.[14] His mentioning of great men demonstrates once more that the call for change pierced the very heart of the alma mater and divided the university corps. It is remarkable that Boerhaave probably suffered a myocardial infarction prior to a period with heart failure, without knowing it, but that is not an issue here.[15]

Figure 2. Herman Boerhaave and family depicted. Those who have an eye for it will notice the abdominal adiposity and a light flush as risk factors avant la lettre.

To give an idea of the divergence in the development of the clinical aspects of cardiology we should mention Jean-Baptiste Senac (1693-1770) who became physician to Louis XV of France and Madame de Pompadour. At a time that Boerhaave hardly made any reference to specific heart diseases, he published already in 1749 his *traite de la structure du coeur, de son action et de ses maladies.* Senacs treatise is considered a landmark in the history of cardiology and commented on the difficulties experienced by physicians in the diagnosis and treatment of heart disease and contributed largely to the resolution of some of these difficulties.[16]

One of the pupils of Boerhaave was Albrecht von Haller (1708-1777) who became professor of anatomy, medicine and botany at the new University of Groningen in 1736. He successfully employed injection techniques to investigate the distribution of blood vessels in the human body and characterised the atrioventricular valves as folds in the endocardium continuous to an atrioventricular ring.[17] His major and influential *Elementa Physiologica* was published between 1759 and 1766 in eight volumes, and was preceded by two publications in 1754 and 1756 which dealt specifically with the cardiovascular system.

An additional source of information about the state of clinical medicine is the premature health registrations which were published in the local newspapers at the end of the 18th century. Obviously infectious diseases then formed a principal part with extremely high mortality rates among children (<10 years) and the elderly (>60 years). Cardiovascular disease was not noted.[18] In 1866 the first national registry on mortality still differentiated only between smallpox, rubella, measles, typhoid fever, diphtheria, cholera and an unknown category. Nevertheless already in 1862 new regulations regarding the medical examination of recruits made use of a long list of ailments and infirmities, and differentiated between a number of cardiovascular diseases such as pericarditis, hydrothorax (borstwaterzucht), hydrops pericardii and organic heart disease including morbus coeruleus (blaauwzucht) and angina pectoris (hartvang).[19] So it is clear that in the beginning of the 19th century there was a foundation for the development of clinical cardiology, but this 'heart house' consisting of anatomy, physiology and pathophysiology still had to be erected, not to say furnished with a proper diagnosis, decision making and effective therapy. It would take another century to reach firm ground with the help of the industrial revolution, technological advance and the socio-geographical and socio-cultural factors connected with this trend. They would eventually shape clinical cardiology as we know it today.

The truth is important because it defines what we believe in

One of the instruments that soon became the ultimate symbol of medical profession is of course the stethoscope. Laennec's (1781-1826) book, *De l'auscultation mediate*, describing his methods, the wooden stethoscope and the different sounds he perceived was published in 1819. Furthermore this work provided a thorough explanation of the important heart and lung diseases in relation to post-mortem findings. In Holland the stethoscope only became common knowledge in 1849 after the translation of a treatise on auscultation from Joseph Skoda (1805-1881) who lectured in Vienna.[20] He was the first to distinguish reverberations (heart sounds) from cardiac

Figure 3. Laennec teaching the use of his stethoscope: learning by doing.

murmurs. On the basis of comparative observations of healthy people and those known to have heart disease he learned to diagnose various heart illnesses from the presence of murmurs in individual valves. At the end of the 19th century the relation between cardiac pathology and different heart sounds was common knowledge. Debate then started on the origin of heart sounds and murmurs, whether or not they are related to the closure or the tension of the semilunar valves[21] and how far the relative contribution of vibrations and whirls (known as tourbillions) reach in the case of the audible mitral valve.[22]

A literally brand new line of development started with the ultimate recognition of coronary insufficiency. Specific circumstances at the time, such as the relative isolation in Napoleonic wartime and a lead in industrialisation with changing lifestyle characteristics, were responsible for the English signature. William Heberden (1710-1801) described angina pectoris as a clinical entity in 1768 and as early as 1778 Edward Jenner (1749-1823) connected angina pectoris with coronary changes found post-mortem which were not confined to simple calcification. Adam Hammer (1818-1878) then gained credit by the description of a cardiac infarction, diagnosed *in vivo*.[23] The famous writer, Heinrich Heine

Figure 4. A photographic portrait of Karl Friedrich Wenckebach. Many advances in photographic glass plates and printing were made throughout the 19th century and in 1884 film technology reached firm ground.

(1797-1856), probably did not relate to this chain of events when he claimed that he would establish himself in the Netherlands if the world ended because in the Netherlands everything occurred 50 years later than in the rest of the world, but the fact remains that one of the first theses on angina pectoris was published in Holland in 1841.[24] At first there were many misapprehensions of this new clinical syndrome when Heberdens accounts were not read carefully enough and others departed from his original delineation. Some related anatomical changes of heart and blood vessels to the angina syndrome but others considered them coincidental. They rather compared angina pectoris with stomach ache. Increasing physiological knowledge of the innervation of the heart then got the upper hand in the explanation of the origin of pain in angina pectoris at the end of the 19th century. Different modifications in the contractility of the heart were believed to cause pain at the same time, throwing light on the complaints in nervous palpitations and valvular pathology too. In this line of thought sympathicotony was considered to play a key role. At the time therapies for the actual attack and during symptom-free intervals were already distinguished. For some time the effect of electricity on various medical cases was already subject of investigation[25] and for a while application of a continuous electric current was considered the therapy of choice during symptom-free periods.[26] In the case of acute pain opiates with digitalis, peppermint water, sulphur combined with vinegar ether, and even chloroform inhalations were applied with more or less success until their fate was decided in favour of the nitrates, first prescribed by Thomas Lauder Brunton (1844-1916).[27]

In the meantime and down the scientific wind from the East, Dutch scholars continued doing what they felt doing best, researching physiology. So Theodor Wilhelm Engelmann (1843-1909), a German physiologist who became a professor at the Utrecht University in 1888, demonstrated the automaticity of heart activity without interference of an external nerve stimulus, as was previously believed.[28] And then following his steps, one of the greatest minds in cardiovascular medicine and a key figure to come of Dutch cardiology, made his appearance. Karl Friedrich Wenckebach (1864-1940), in whose honour The Netherlands Society of Cardiology (NVVC) was founded on his 70th birthday (28 april 1934), made his famous contribution on arrhythmias of the heart in 1904.[29] Previously he had published on the nature and the significance of extrasystoles with the help from pulse recordings.[30] A second paper dealt with the conduction delay that brought about a phenomenon like the pulsus regulariter intermittens, better known as the Wenckebach phenomenon.[31]

Conclusion

It seems that the Enlightment triggered two crude lines of development in cardiology, which of course interacted. A French-Anglo-Saxon pathway, more practical and clinically orientated and a second continental way dominated by natural science and the quest for truth. Both routes merged again in the early 20th century when the discovery of electrocardiography became the starting point for an interactive roller coaster ride in cardiovascular medicine, the end of which is not foreseen yet. It is important to know about these time travels and the ongoing and irreversible technological advance which is exciting and terrifying at the same time. Knowing history puts things into perspective and helps to find the necessary balance between human needs and dignity. ■

References

1 McCall H. Gilgamesh and the flood. Mesopotamian Myths. British Museum Publications: 45. London 1990.
2 Harris CRS. The heart and the vascular system in ancient Greek medicine. Oxford University press 1973; chapter 7:397-432.
3 Van Tellingen C. An anatomy lesson and the quality of intermittence. *Neth Heart J* 2007;**15**:239-41.
4 www.iisg.nl/hpw/calculate.php
5 Cook HJ. Matters of exchange, commerce, medicine and science in the Dutch Golden Age. Yale University Press 2007; 164-71.
6 Van Leeuwenhoek A. Brieven. Cornelis Boutesteyn, Boekverkoper 't Rapenburg, Leyden. 1st edition 1688. p 308.
7 Lindeboom GA. William Harvey en zijn ontdekking van de bloedsomloop. N*ed Tijdschr Geneeskd* 1957;**101**:2209-15.
8 Bouckaert J. Steven Blankaart (1650-1704) auteur van het eerste Nederlandstalige boek over kinderziektes. *GdG* 2008;12:165-75.
9 Modlin IM. The medical legacy of Leiden. Precision Collection of Dutch Medicine. 1998. p 40.
10 Van Lieburg MJ. Voetius en de geneeskunde. Claves Pietatis 2007;168-180.
11 Wenckebach KF. William Harvey en de ontdekking van den bloedsomloop. *Ned Tijdschr Geneeskd* 1911;55:1444-58.
12 Kooijmans L. Gevaarlijke kennis. Inzicht en angst in de dagen van Jan Swammerdam. Uitgeverij Bert Bakker. Amsterdam 2007; chapter I and II: 1-49.

13 Schweikardt CJ. Ten strijde tegen de galenische behandelwijzen. *GdG* 2001;7:228-35.
14 Boerhaave H. Kortbondige spreuken wegens de ziektens, ingeleid door Lindeboom GA. Stafleu's wetenschappelijke uitgeversmaatschappij bv. Alphen aan den Rijn. 1979. Voorreeden p. 3.
15 Modlin IM. The medical legacy of Leiden. Precision Collection of Dutch Medicine. 1998. p. 47-59.
16 Fleming PR. A Short History of Cardiology. Rodopi. Amsterdam/Atlanta GA. 1997. p. 7-11.
17 Modlin IM. The medical legacy of Leiden. Precision Collection of Dutch Medicine. 1998. p. 77-82.
18 's Hertogenbossche Vrydagse Courant Den 18 January 1783. Brabant Collectie. Tilburg University.
19 Staatsblad 1862 (no. 34) from p. 25.
20 Skoda J. Abhandlung über Perkussion und Auskultation. Ritter von Mösle Witwe & Braumüller, Vienna 1839. 6th edition, 1864.
21 Stokvis BJ. Eene eenvoudige proef met betrekking tot het aandeel der klapvliezen aan het verwekken der harttonen. *Ned Tijdschr Geneeskd* 1880;**24**:613-8.
22 Feltkamp TEW. Enkele opmerkingen over harttonen en hartgeruischen. *Ned Tijdschr Geneeskd* 1893;**37**:33-9.
23 Hammer A. Thrombotischem Verschlusse einer der Kranzarterien des Herzens. Wiener Medizinische. Wochenschrift 1878;**5**:97-102.
24 Vos Houwink A. Nonnula de angina pectoris. 1841.
25 Callender GW. Notes of clinical lecture of some cases in which the continuous electric current was used. *Br Med J* 1872;**1**:149-50.
26 Browne J. Twee gevallen van angina pectoris. *Ned Tijdschr Geneeskd* 1886;**31**:109-43.
27 Brunton Lauder T. Pharmacology and Therapeutics, or, Medicine Past and Present. Macmillan and Company. London, 1880,
28 Engelmann TW. Ueber die Leitung der Bewegungsreize im Herzen. Onderzoekingen Physiol. Labor. Utrecht. Series IV. Part III. 1894.
29 Wenckebach KF. Arrhythmia of the heart; a physiological and clinical study, translated by Snowball T. W. Green. Edinburgh. 1904.
30 Wenckebach KF. De analyse van den onregelmatigen pols. *Ned Tijdschr Geneeskd* 1898;**42:**297-316.
31 Wenckebach KF. De analyse van den onregekmatigen pols. II over den regelmatig intermitteerende pols. *Ned Tijdschr Geneeskd* 1899;**43**:665-79.